the composition provides a ratio of non-protein calories per gram nitrogen of at least approximately 90:1.

Please cancel claims 4 and 16 without prejudice or disclaimer.

REMARKS

In the Office Action, claims 1-22 are stand rejected and are provisionally rejected under the judicially created doctrine of obviousness–type double patenting; and claims 1-22 are rejected under 35 U.S.C. §§ 102 and/or 103. Claims 1, 7, 14 and 19 have been amended and claims 4 and 16 have been cancelled. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with Markings to Show Changes Made**." Applicants respectfully submit that the rejections have been overcome for the reasons set forth below.

At the outset, the Examiner asserts that the Terminal Disclaimer does not comply with 37 C.F.R. § 1.321 as previously filed. In this regard, the Patent Office asserts that the disclaimer fee of $110.00 has not been submitted, nor is there any authorization in the application file to charge a specified deposit account or credit card. Although Applicants believe that the Patent Office's position is incorrect, in the spirit of cooperation and to expedite closure of this issue, Applicants are submitting herewith a check in the amount of $110.00 to cover the submittal fee for the Terminal Disclaimer. Therefore, Applicants believe that this issue should be resolved.

In the Office Action, claims 1-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being patentable over claims 1-30 of U.S. Patent No. 5,661,123; claims 1-22 of U.S. Patent No. 6,200,950; and claims 1-20 of U.S. Patent No. 5,549,905. At the outset, Applicants submitted a Terminal Disclaimer in response to this rejection raised in the Office Action dated March 26, 2002. As previously discussed, the Patent Office asserts that the Terminal Disclaimer does not comply with 37 CFR §1.321. In the spirit of cooperation, Applicants are submitting herewith a check in the amount of $110.00. Thus, Applicants believe that the Terminal Disclaimer is in compliance with 37 CFR §1.321.

Accordingly, Applicants respectfully request that the rejection of claims 1-22 under the judicially created doctrine of obviousness-type double patenting be withdrawn.

In the Office Action, claims 1-22 are provisionally rejected under the judicially created doctrine of obviousness–type double patenting as being unpatentable over claims 1-22 of co-pending U.S. Patent Application No. 09/622,629. In response, Applicants respectfully submit that upon Notice of Allowability of either one of the co-pending applications that a Terminal Disclaimer will be filed to address this rejection. Therefore, Applicants believe that they have been fully responsive to this provisional rejection.

In the Office Action, claims 1-12, 14-20 and 22 are rejected under 35 U.S.C. § 102 as being anticipated by U.S. Patent No. 5,221,668 ("*Henningfield*"). Applicants believe that *Henningfield* is clearly deficient with respect to the claimed invention as discussed in detail below.

Of the presently pending claims, claims 1, 7, 14 and 19 are the sole independent claims. Each of these claims have been amended as fully supported in the Specification. No new matter has been added. Claim 1 recites an enteral composition; claim 7 recites a method for providing nutrition to a metabolically stressed patient; claim 14 recites an enteral composition for a metabolically stressed patient; and claim 19 recites a method for providing nutrition to a metabolically stressed patient. The nutritional composition of the present invention includes, in part, a protein source consisting of enzymatically hydrolyzed whey and free amino acids wherein the protein source provides approximately 15% to 18% of energy of the composition. Further, the composition includes a carbohydrate source, a lipid source wherein the composition has a caloric density of 1.4 kcal/mL to 1.8 kcal/mL and wherein the composition provides a ratio of non-protein calories per gram of at least 90:1.

The claimed invention provides a product that is specifically directed to meet nutritional needs of metabolically stressed patients without elevated protein levels or excess fluid. To this end, the claimed invention provides calorically dense nutritional support in the form of an enteral composition while at the same time providing a moderate non-protein calories per gram of nitrogen ("NPC/gN") ratio. The nutritional diet of the claimed invention utilizes whey subjected to enzymatic hydrolysis used as a protein source, thus yielding peptides and free amino acids.

Further, amino acids may be added in small amounts in the form of free amino acids. This can enhance absorption in the metabolically stressed patients. See, Specification, Page 6, line 23 to Page 7, line 4. As previously discussed, the enteral composition of the claimed invention includes, in part, a caloric density of at least 1.4 kcal/mL wherein the composition provides a ratio of non-protein calories per gram of nitrogen of at least 90:1. The composition can further include, in part, a protein source that provides about 15% to about 18% of the calorie distribution of the composition. For adults and older children (10 plus years or older), for example, the protein concentration of the claimed invention is optimal for the moderate tissue repair needs of the targeted patient populations without imposing an undue nitrogen burden on renal function. See, Specification, Page 4, lines 4-17.

Further, Applicants are submitting herewith additional scientific evidence that demonstrates the desirable characteristics of the present invention. In this regard, the scientific evidence is provided in the form of scientific publications attached hereto as Exhibits A-F. In general, the scientific evidence is based on a comparison of two types of nutritional formulas, namely, PEPTAMEN 1.0® and PEPTAMEN 1.5® which are administered to patients who are in a state of metabolic stress in urgent need of increased energy according to an embodiment of the present invention. As detailed below, the scientific evidence demonstrates that patients prefer the high energy formula made in accordance to an embodiment of the present invention because feeding time and feeding amount was reduced, thus allowing for other activities to take place, such as going to school.

For example, Exhibit A provides a study conducted on a 14-year old female with an 8-year history of Crohn's disease. After transition from 1.0 to 1.5 cal/cc formula, feeding time was reduced by more than 50%; the subject could go to school; and the subject experienced a 32% weight gain. See, *J. M. Murdy et al.*, HIGH CALORIE ELEMENTAL DIET IMPROVES OUTCOMES AND QUALITY OF LIFE FOR TUBE FED ADOLESCENTS, Abstract (1999).

As disclosed in Exhibit B, a woman of 21 years and pregnant for 28 weeks (RK) suffered a malrotation of the small intestine. After months of hospitalization, she received a quadruple organ transplant of the small bowel, liver, kidney and pancreas. RK immediately started feeding with a powdered amino-acid based, liquid formula which was poorly tolerated. The formula was

changed to a formula according to an embodiment of the present invention which was immediately tolerated. Within a year, RK's weight returned from 117 to 130 lbs. See, Exhibit B, *R. S. Kindle et al.*, HIGH CALORIE PEPTIDE-BASED, LIQUID, ELEMENTAL, ENTERAL FORMULA IS WELL-TOLERATED BY PATIENT WITH QUADRUPLE ORGAN TRANSPLANT, Abstract (2002).

As disclosed in Exhibit C, a 42-year old male with chronic pancreatitis, irritable bowel and a history of alcohol abuse was maintained on total parentral nutrition for 14 weeks. Despite increasing energy intake, he lost weight.

The diet was then changed to a 1.0 kcal/mL and later to the 1.5 kcal/mL whey-based peptide diet according to an embodiment of the present invention. The formula change and increased energy intakes were well tolerated. Liver enzymes returned to normal within four weeks of the enteral therapy and the patient gained weight. See, Exhibit C, *J. Meyer*, HOME ENTERAL NUTRITION IN CHRONIC PANCREATITIS: A CASE REPORT, Support Line, pp. 7-10 (2000). *J. Meyer et al.*, ENTERAL NUTRITION IN CHRONIC PANCREATITIS: COST SAVINGS WITH THE USE OF A 1.5 KCAL/ML PEPTIDE-BASED DIET, Abstract (1999).

As disclosed in Exhibit D, children suffering from Chrohn's disease were normally given a 1 kcal/mL standard defined formula that had to be consumed in a large volume. A retrospective analysis was performed to evaluate the effect of the use of condensed semi-elemental diet (a 1.5 kcal/mL diet made in accordance with an embodiment of the present invention) on the acceptability, tolerance, weight gain and efficacy of nutritional therapy for pediatric CD patient. Patients preferred the reduced volume of condensed product required to meet their nutritional needs. See, Exhibit D, *L. Bouthiller et al.*, USE OF CONDENSED SEMI-ELEMENTAL DIET IN THE TREATMENT OF PEDIATRIC CROHN'S DISEASE, p. 74 (2002).

As disclosed in Exhibit E, gastric emptying rate of equal volumes of two whey-based formulas of different energy density and osmolality was studied in ten children ranging in age from 4½ to 12 years. Gastric emptying rates of the two formulas were comparable. Over a one-month clinical trial, substitution of the lower energy density whey-based formula with an equal

volume of the high density formula produced a mean-weight gain of 1.17 kg per patient without change in tolerance. See, Exhibit E, *V. Khoshoo*, GASTRIC EMPTYING OF TWO WHEY-BASED FORMULAS OF DIFFERENT ENERGY DENSITY AND ITS CLINICAL IMPLICATION IN CHILDREN WITH VOLUME INTOLERANCE, European J. of Clinical Nutrition, v. 56, pp. 1-3 (2002).

As disclosed in Exhibit F, children suffering from cystic fibrosis (CF) were given the formula according to an embodiment of the present invention. All four children experienced weight gain. See, *J. A. Fulton, et al.* USE OF A READY-TO-FEED, SEMI-ELEMENTAL FORMULA FOR GASTRONOMY TUBE FEEDINGS IN CHILDREN WITH CYSTIC FIBROSIS, Abstract 77 (1999).

In view of same, Applicants respectfully submit that the scientific evidence clearly demonstrates the beneficial effects of the present invention. Therefore, Applicants respectfully request that the Examiner consider such evidence upon reconsideration and evaluation of the present invention in view of the cited art.

In contrast, *Henningfield* fails to disclose or suggest a number of features of the claimed invention. Of course, an anticipation rejection requires that "there must be no difference between the claimed invention and a reference's disclosure as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). Accordingly, "for a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." *In re Bond*, 910 F.2d 831 (Fed. Cir. 1990).

Applicants believe that *Henningfield* at least fails to disclose or suggest an enteral composition that includes, for example, a protein source consisting of hydrolyzed whey and free amino acids wherein the enteral composition has a caloric density of at least 1.4 kcal/mL and wherein the composition provides a ratio of non-protein calories per gram of nitrogen of at least 90:1 as required by the claimed invention. For example, the preferred caloric density of the nutritional product in *Henningfield* is 1.3 kcal/mL. See, *Henningfield*, column 9, lines 10-12.

Further, Applicants believe that *Henningfield* is deficient with respect to a protein source limited to hydrolyzed whey and free amino acids as required by the claimed invention. In this

regard, the *Henningfield* reference discloses that hydrolyzed sodium caseinate must be present in a nutritional composition. See, *Henningfield*, column 9, lines 56-58. Indeed, the sodium caseinate is present in higher amounts than the lactalbumin hydrolysate. For example, *Henningfield* discloses 60-70% of hydrolyzed sodium caseinate as compared to 20-30% of lactalbumin hydrolysate. See, *Henningfield*, column 9, lines 62-68. This clearly suggests that one skilled in the art viewing *Henningfield* would not be inclined to increase the amount of hydrolyzed whey in a nutritional formula up to the extent of the enteral composition that consists of hydrolyzed whey and free amino acids as required by the claimed invention.

Moreover, Applicants believe that *Henningfield* is deficient with respect to an enteral composition that has a protein source of enyzmatically hydrolyzed whey and free amino acids wherein the protein source provides about 15% to 18% of the calorie distribution of the composition as required by the claimed invention. As previously discussed, Applicants have found that the total amount of energy provided by the protein source of the claimed invention is optimal for moderate tissue repair needs of the targeted patient populations without imposing an undo nitrogen burden on real function. Indeed, *Henningfield* discloses that about 20.5% of the calories provided by protein is most preferred. See, *Henningfield*, column 9, lines 28-29.

The *Henningfield* composition is also intended for trauma patients, especially server injury. See, *Henningfield*, column 1, lines 10-15. In contrast, the enteral compositions of the claimed invention are for metabolically stressed patients, particularly patients that have compromised absorptive capacity. One skilled in the art viewing *Henningfield* would clearly consider *Henningfield,* for at least these reasons, to be deficient with respect to the specific features of the claimed invention. Therefore, Applicants believe that *Henningfield* fails to disclose or arguably suggest the claimed invention.

Accordingly, Applicants request that this rejection be withdrawn.

In the Office Action, claims 1-16 and 18-22 are rejected under 35 U.S.C. § 103 as obvious over U.S. Patent No. 5, 714,472 ("*Gray*"). Applicants believe that *Gray*, like *Henningfield*, fails to disclose or suggest a number of features of the claimed invention.

For example, Applicants do not believe that *Gray*, like *Henningfield*, discloses or suggests an enteral composition for metabolically stressed patients that includes, in part, a protein source of hydrolyzed whey and free amino acids with about 15% to 18% of the energy content of the composition. Indeed, the Examiner admits that *Gray* merely provides "about 22%" of the energy of the composition. See, Office Action, page 7. This is clearly not substantially the same as an enteral composition with a protein energy content of about 15% to about 18%. *Gray* also discloses that the total non-protein calories per gram of nitrogen should be less than or equal to 70:1. This clearly contrasts the claimed invention which requires, in part, a ratio of non-protein calories per gram of nitrogen of at least about 90:1.

Further, the clear emphasis of *Gray* relates to nutritional compositions with a protein source composed of hydrolyzed casein. See, *Gray*, col. 4, line 62. Optionally, *Gray* further discloses that hydrolyzed whey may be used in smaller amounts than the hydrolyzed casein. *Gray*, col. 4, line 66. Moreover, Applicants have provided scientific evidence that demonstrate the beneficial effects of the specific nutritional properties of the present invention as previously discussed. Therefore, Applicants believe that *Gray* is clearly deficient with respect to the claimed invention.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

In the Office Action, claims 1-22 are rejected under 35 U.S.C. § 103 as being unpatentlable over U.S. Patent No. 5,166,189 ("*Trimbo*") in view of U.S. Patent No. 5,504,072 ("*Schmidl*"), *Gray*, U.S. Patent No. 4,427,658 ("*Maubois*") and further in view of *Granger et al.* The Patent Office primarily relies on *Trimbo* and thus relies on the other cited references to remedy its deficiencies.

In contrast, the cited art fails to disclose or suggest a number of features of the claimed invention. With respect to *Trimbo*, Applicants believe that this reference is clearly deficient with respect to a number of features of the claimed invention even as admitted by the Examiner. See, Office Action, page 6.

For example, *Trimbo* is deficient with respect to an enteral composition suitable for metabolically stressed patients that includes, in part, a protein source of hydrolyzed whey and

free amino acids wherein the protein source provides about 15% to 18% of the energy content wherein the composition has a caloric density from 1.4 kcal/mL to 1.8 kcal/mL. Indeed, *Trimbo* discloses, for example, that the composition has an energy content of 1.2 kcal/ml. Further, *Trimbo* discloses that not less than 18% of the energy may be provided by protein. Moreover, nowhere does *Trimbo* disclose or suggest the use of hydrolyzed protein.

As previously discussed, the claimed invention provides an enteral composition that includes a protein source consisting of both hydrolyzed whey and free amino acids and that provides about 15% to 18% of the total energy of the composition wherein the enteral composition has a caloric density that ranges from 1.4 kcal/mL to 1.8 kcal/mL. The claimed invention provides a calorically dense nutritional support in the form of an elemental diet while at the same time providing a moderate NPC/gN ratio specifically directed to meet the nutritional needs of metabolically stressed patients without elevated levels or excess fluid. See, Specification, Page 6, lines 23-28. Therefore, Applicants believe that *Trimbo* is clearly deficient with respect to the claimed invention.

Further, the remaining references, even if combinable, cannot remedy the deficiencies of *Trimbo*. For example, nowhere do any of these references, alone or in combination, disclose or suggest the protein energy content and caloric density features of the claimed invention. Indeed, *Schmidl* fails to disclose or suggest, for example, an enteral composition that has a caloric density of 1.4 kcal/mL to 1.8 kcal/mL as required by the claimed invention. In contrast, *Schmidl* states "the composition can also be in the form of a ready-to-use aqueous liquid which preferably has a caloric content of 1 kcal/mL." See, *Schmidl* column 7, lines 54-57.

If anything, *Schmidl* teaches away from the claimed invention. The mere fact that a composition has lipids, carbohydrates, and protein does not mean the composition has the same caloric density as another composition including lipids, carbohydrates, and proteins. Simply because a product has lipids, carbohydrates, and protein does not mean it has the same characteristics as another product having lipids, carbohydrates, and protein. There are millions of compositions including a lipid, a carbohydrate, and a protein that have different properties.

Further, *Schmidl* fails to disclose or suggest an enteral composition with a protein source that consists of enzymatically hydrolyzed whey and free amino acids. The clear emphasis of

Schmidl relates to compositions with free amino acids. Moreover, *Schmidl* merely and only generally discloses that hydrolyzed or intact proteins may be present. See, *Schmidl*, col. 4, lines 1-2. Therefore, Applicants believe that *Schmidl* is clearly deficient with respect to the claimed invention.

With respect to *Gray*, this reference discloses a protein source energy content that is clearly outside of the scope and content of the claimed invention as discussed above.

Contrary to the Patent Office's position, *Maubois* fails to disclose or suggest, for example, protein intake ranging from 7% to 25% of the total caloric intake. Examples 5 and 6 merely suggest that the protein intake can be 7% to 12% (Example 5) or 25% of the total caloric intake. This is clearly does not suggest the protein energy content of 15% to 18% as required by the claimed invention. Moreover, the Patent Office merely relies on *Granger* for its purported teaching relating to providing elemental protein to hypermetabolically stressed patients.

Based on at least these differences, the cited art, even if combinable, is clearly deficient with respect to a number of features of the claimed invention. Again, Applicants have provided scientific evidence to demonstrate the beneficial effects of the specific nutritional properties of the claimed invention. In view of same, Applicants believe that one skilled in the art viewing *Trimbo*, even if combinable with any one or all of the other cited references, would not be inclined to modify *Trimbo* to arrive at the claimed invention. Therefore, Applicants believe that the cited art, even if combinable, fails to render obvious the claimed invention.

Accordingly, Applicants respectfully request that the obviousness rejection be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the present application and earnestly solicit allowance of same.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1, 7, 14 and 19 have been amended as follows:

1. (Amended) An enteral, peptide-based composition comprising:

a protein source consisting of enzymatically hydrolyzed whey ~~protein~~ and free amino acids wherein the protein source provides approximately 15% to 18% of energy of the composition;

a carbohydrate source; and

a lipid source including a mixture of medium and long chain triglycerides, the enteral composition having a caloric density of ~~at least~~ 1.4 kcal/mL to 1.8 kcal/mL, wherein the composition provides a ratio of non-protein calories per gram nitrogen of at least 90:1.

7.(Amended) A method for providing nutrition to a metabolically stressed patient comprising the step of administering to the patient a therapeutically effective amount of an enteral, peptide-based composition comprising:

a protein source comprising approximately 15% to ~~about 20~~18% of the calorie distribution of the composition, the protein source consisting of enzymatically hydrolyzed ~~protein~~ whey and free amino acids;

a carbohydrate source;

a lipid source ;

the enteral composition having a caloric density of ~~at least~~ 1.4 kcal/mL to 1.8 kcal/mL; and

the composition provides a ratio of non-protein calories per gram nitrogen of at least approximately 90:1.

14.(Amended) An enteral, peptide-based composition for a metabolically stressed patient comprising:

about 15% to ~~about 20~~18% of the calorie distribution of the composition including a protein source consisting ~~essentially~~ of enzymatically hydrolyzed whey ~~protein~~ and free amino acids;

a carbohydrate source comprising at least 35% of the composition;

a lipid source comprising at least 20 by weight of the composition; and

the composition having a caloric density of ~~at least~~ 1.4 kcal/mL to 1.8 kcal/mL and a ratio of non-protein calories per gram of nitrogen of at least about 90:1.

19.(Amended) A method for providing nutrition to a metabolically stressed patient comprising the step of administering to the patient a therapeutically effective amount of an enteral, peptide-based composition comprising:

a protein source comprising approximately 15% to ~~about 20~~18% of the calorie distribution of the composition, the protein source consisting ~~essentially~~ of enzymatically hydrolyzed whey ~~protein~~ and free amino acids;

a carbohydrate source;

a lipid source ;

the enteral composition having a caloric density of ~~at least~~ 1.4 kcal/mL to 1.8 kcal/mL; and

the composition provides a ratio of non-protein calories per gram nitrogen of at least approximately 90:1.

Claims 4 and 16 have been cancelled.